COST ACTION BM 1105 “GNRH DEFICIENCY: ELUCIDATION OF THE NEUROENDOCRINE CONTROL OF HUMAN REPRODUCTION”

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Abstract

COST (European Cooperation in Science and Technology) is an intergovernmental organization established to fund research networks known as “COST Actions” across the sciences. COST enables break-through scientific developments leading to new concepts and products and thereby contributes to strengthen Europe’s research and innovation capacities. The Action BM1105 investigated the neuroendocrine mechanisms that are integrated at the hypothalamic level and regulate the complex organ network controlling reproduction. Through the development of a networking platform, the Action advanced the field of neuroendocrinology *via*: guidelines for the best clinical care of GnRH deficient patients, translating scientific understanding into improved patient care and creating a lasting European tradition of excellence in the field of reproductive medicine.

Key words: COST Action BM 1105, hypogonadotropic hypogonadism.

INTRODUCTION

COST is an intergovernmental framework for European Cooperation in Science and Technology, allowing the coordination of nationally-funded research on a European level and is a unique means for European researchers to jointly develop their own ideas and new initiatives across all scientific disciplines. A COST Action represents a network of nationally funded projects based on a Grant Agreement, a joint work and a budget plan of at least 5 countries, cross 9 Domains or interdisciplinary. Biomedicine and Molecular Biosciences (BMBS) domain covers all areas of medicine in Europe including fundamental, preclinical and clinical medical research developed to materialise the “bench to bedside” concept.

COST instruments are: meetings, Short-Term Scientific Missions (STSMs), training schools, dissemination (scientific publication, action website,

action promotion for meetings and training schools and outreach activities), early stage researcher conference grant and strategic activities.

The COST Action BM 1105 “GnRH deficiency: Elucidation of the neuroendocrine control of human reproduction” aims to investigate the neuroendocrine mechanisms that are integrated at the hypothalamic level and regulate the complex organ network controlling reproduction. Implicated genes/pathways have been identified through genetic investigations of rare patients with isolated GnRH deficiency, who display reproductive failure. Despite knowledge of 16 disease genes, multiple additional genes and mechanisms remain undiscovered, requiring higher-order collaborations for full elucidation. Through a collaborative network of physician-scientists and biologists, the Action’s aims were to deliver: a database with de-identified genetic and phenotypic data on at least 1.000 GnRH-deficient patients, their families, and unaffected controls; one or more disease gene(s) in each patient, and/or 10 or more novel disease genes; elucidation of newly identified genes’ roles in animal/cell-based systems and guidelines for genetic counselling of GnRH-deficient patients based on the emerging disease architecture.

The action started in April 2012 and ended in April 2016; 35 European countries have participated in this project, Romania being invited to adhere at the beginning of 2012. Specific objectives that will be addressed by over the four years of the project included:

- Reach out to and include clinicians, physician scientists, genetic counsellors, and basic researchers from all European countries;
- Recruit collectively a cohort of at least 1,000 well phenotyped patients with GnRH deficiency, and create a common web - accessible database for storing the identified genetic and phenotypic data on patients;
- Facilitate the joint investigation of specific patients/families with unique phenotypes identified

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through the database (deliverable: joint clinical and scientific research projects; publications);

- Facilitate access to and shared use of cutting-edge platforms for genetic research (deliverable: genetic studies, publications);

- Fully describe the phenotypic spectrum of GnRH deficiency (including its response to hormonal treatment) and to delineate the underlying genotype-phenotype correlations;

- Create genetic counselling guidelines for GnRH deficient patients and their family members based on the emerging disease architecture (deliverable: genetic counselling guidelines, endorsement by medical society, publication);

- Connect adult and pediatric endocrinologists to optimize therapeutic approach for patients in transition between childhood and adulthood, and to share clinical experience/protocols to identify the influence of hormonal regimens on clinical endpoints such as quality of life and fertility (deliverables: clinical treatment guidelines, endorsement by medical society, publication);

- Recruit and train 100 or more young investigators in reproductive research (deliverables: Training School participation and full-time research/fellowship positions);

- Facilitate joint applications for national and European funding (deliverable: research supporting grants);

- Reach out to patients, their families, and patient advocacy groups to provide support, education and expert clinical care (deliverable: online, telephone and in person interaction capabilities at the national level as well as across the network).

In order to accomplish these objectives, the network was organized in 4 different Working Groups which had representatives in each participating country. These working groups were: Clinical Working Group, Genetics/bioinformatics Working Group, Basic Science Working Group and Education Working Group. Romania had at least 1 member in each of these working groups.

At the National level: eight Romanian clinical investigators, bio scientists and young researchers

had their professional profiles posted on the Action website. Our country had representatives at each of the scientific events organized during the Action. There are 37 patients with hypogonadotropic hypogonadism enrolled into the database at “C.I. Parhon” National Institute’s level. The patients were clinical and biochemical characterized using a specific evaluation protocol elaborated by clinicians from “C.I. Parhon” National Institute of Endocrinology and then used nationwide. The DNA extraction was performed in our lab and we hope for a better interaction with geneticists from other countries, in order to identify the specific genetic mutations in all our patients.

At the European level: the website has been launched (www.gnrhnetwork.eu), investigator profiles have been posted and parameters for phenotypes have been established for the patient registry. Through the development of a networking platform, the Action advanced the field of neuroendocrinology *via*: evidence based guidelines for the best clinical care of GnRH deficient patients, translating scientific understanding into improved patient care training the next generation of investigators, creating a lasting European tradition of excellence in the field of reproductive medicine, enhanced capacities for responding to funding calls at both the national and EU levels.

In conclusion, COST action BM 1105 performed its goals: build a European network to foster collaboration on the theme of Hypogonadotropic Hypogonadism, identify genes and mechanisms regulating the neuroendocrine control of human reproduction, inform and validate human studies using corresponding animal and cellular models, translate findings into improved patient care, genetic counselling, create a harmonized patient registry, develop a website with the listing of specialized European centres, create guidelines for diagnosis, treatment and genetic counselling, train the next generation of investigators and provide patients advocacy and support.

Conflict of interest

The author declares that she has no conflict of interest concerning this article.